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ARTERIO-VENOUS ANASTOMOSES AND THERMOREGULATION

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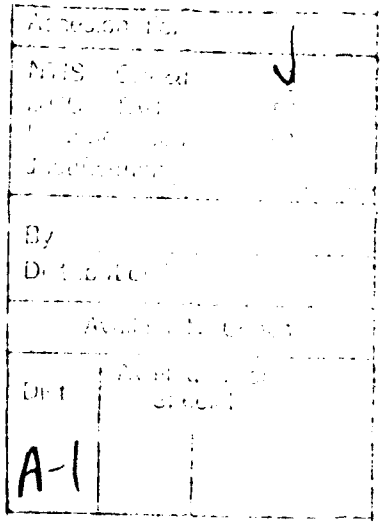

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SUMMARY

In a cold environment human heat loss is reduced by peripheral vasoconstriction, counter-current heat exchange and a change of the peripheral circulation pattern. However, these mechanisms go at the expense of the tissue temperature in the extremities. The cooling can be so pronounced that local cold injuries occur. Cold induced vasodilation (CIVD) may be regarded as an effective protection against local cold injury. The underlying mechanism is often associated with the presence of arterio-venous anastomoses (AVA). Rhythmic relaxation and contraction of the strong muscular wall of the AVA is often supposed to cause the 'hunting' response in CIVD. The contraction phase is probably caused by stimulation of the α-adrenoceptors in the smooth muscle wall. Relaxation may be caused by a nervous blockade of the sympathetic system. There is no scientific evidence for humeral mediators. The influence of the body temperature on the vasomotor tone of the AVA remains to be investigated. The locations of AVA and the sites where CIVD occurs are not in perfect correspondence and also this point needs further research.

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Arterio-veneuze anastomosen en thermoregulatie

H.A.M. Daanen

SAMENVATTING

In een koude omgeving probeert de mens zijn warmteverlies zo veel mogelijk te beperken door perifere vasoconstrictie, arterio-veneuze tegenstroom en een verandering van perifeer circulatiepatroon. Deze mechanismen gaan echter ten koste van de weefseltemperatuur in de extremiteiten. De afkoeling kan zo sterk zijn, dat er koude letsels ontstaan. Cold-induced vasodilation (CIVD) kan worden gezien als een effectieve bescherming tegen lokaal koudeletsel. Het achterliggende mechanisme is vaak in verband gebracht met de aanwezigheid van arterio-veneuze anastomosen (AVA). De ritmische samentrekking van de gespierde wand van de AVA wordt gezien als de oorzaak van de 'hunting response' in CIVD. De contractiefase wordt verklaard door stimulatie van de α-receptoren in het membraan van de gladde spiercellen. Relaxatie kan verklaard worden door een nerveuze blokkade van het sympatische systeem. Er is geen hard bewijs voor humerale mediatoren. De invloed van de lichaamstemperatuur op de tonus van de spieren rondom de AVA moeten nog diepgaand worden onderzocht. De plaatsen waar AVA worden aangetroffen en waar CIVD wordt aangetoond komen trouwens niet perfect overeen, zodat ook daar nader onderzoek gewenst is.

1 INTRODUCTION

The Thermal Physiology research group of the TNO Institute for Perception has a special interest in the pathology of cold injuries.
Freezing and non-freezing injuries can be distinguished. In the latter a prolonged exposure to wet cold leads to nerve and tissue damage, which may cause a lot of pain. The trenchfoot is the most common example of a non-freezing cold injury.
In a cold environment the hand and foot are most prone to cold injuries because the blood flow is drastically reduced there to prevent heat loss. However, in some places of the human body this reduction in peripheral blood flow is followed by an increased flow after several minutes. This mechanism is called cold induced vasodilation (CIVD) and is supposed to be a safety mechanism to prevent cold injuries.
The occurrence of CIVD is attributed to the opening of arterio-venous anastomoses (AVA). Arterio-venous anastomosis are blood vessels in the subcutis which form a direct connection between the arterial and venous system. When they are opened a great amount of warm blood may pass through this shunt. The blood warms the tissue and thus plays an important role in thermoregulation.
Many topics concerning the function of AVA are still subject to debate. For instance the results from scientific investigations about exact location, the number, the innervation and dilator mechanism of AVA are not univocal.

It is the purpose of this report to review the literature concerning the role of AVA in thermoregulation.

2 SHORT-TERM CIRCULATORY ADJUSTMENTS TO A COLD ENVIRONMENT

As soon as a subject enters a cold environment several mechanisms are triggered to increase metabolism and to prevent heat loss to the surroundings. The reduction in heat loss is achieved in different ways (Raman & Vanhuyse, 1975):

- **vasoconstriction in the skin**

Burton and Edholm (1955) are the opinion that vasoconstriction in the peripheral musculature also contributes to the prevention of heat loss. They calculated that cooling of the blood leads to an increased viscosity, but that this increase in viscosity alone was insufficient to explain the reduction in peripheral blood flow. Thus vasoconstriction has to be assumed.

- **change of circulation-pattern**

Normally, the connection between the arterial and venous circulation is brought about by capillaries. Capillaries are vessels with a diameter of 5 to 10 μm (Bernards & Bouman, 1978). In some parts of the human body as fingers, lips, cheeks, nose and elbows (Sucquet, 1862 quoted in Hale & Burch, 1960) direct

connections between the arterial and venous network are found. These connections are called arterio-venous anastomoses (AVA). Grant and Bland (1931) investigated the role of AVA in the thermoregulation. They found a relation between the number of AVA in a body part and the change in local skin temperature due to local cold. Since this discovery the importance of AVA for local temperature regulation is often stressed.
The circulation pattern thus can be changed by a different distribution of blood flow through AVA and capillaries.

- **counter current heat exchange (CCHE)**

CCHE means that two adjacent vessels with opposite blood flow direction interchange heat. This CCHE was first described by Bazett et al. (1948) who determined the temperature of the blood inside the radial artery. Following Bazett, the contribution of CCHE to the reduction in heat loss is mainly investigated with analytical models.
Mitchell and Myers' (1968) analytical model revealed that no significant counter-current effect occurred in the arm of man. It is reasonable to assume that for these large vessels the distance between the arterial and venous vessels is too great, the blood flow too fast, and the length of the vessels too short to ensure CCHE.
In the periphery where the arterial and venous vessels are very close, the difference in temperature between the vessels is so small that almost no CCHE occurs. Song et al. (1987) consider the micro vessels thermally insignificant when their dimensions are less than 50 μm.
According to Jiji et al. (1984) the thermally significant counter-current arteries and veins are located in the deep tissue (more than 4 mm under the skin surface) and are 50 to 300 μm in diameter. In this area the combination of vessel length, blood flow and distance between arterial and venous vessels is optimal for CCHE.
Jiji et al. (1984) stress the influence of CCHE by pointing at the very small arterio-venous temperature difference of only 0.1 to 0.2°C, while the difference between the temperature in the major supply vessels and the skin temperature amounts to 5-10°C. Effective rewarming of the blood must have occurred in the way back to the heart.
Vanggaard (1975) argues that CCHE is of minor importance in total heat exchange. He found no difference in temperature decay when a hand was cooled in an occluded and non-occluded situation. He came to the conclusion that CCHE either had to be always 100% effective or negligible, and naturally opted for the latter. However, the 'physiological amputation' of the skin of the hand due to peripheral vasoconstriction leads to a passive elimination of the heat of the hand. It is thus likely that Vanggaard has not been able to detect any CCHE in his tests.
Recently, Raman and Roberts (1989) estimated the effectiveness of CCHE by mathematical modelling. They distinguish between heat conservation in the human hand by a change of the pattern of circulation from cutaneous to deep venous vessels and by CCHE between the artery and deep vein. The change of

circulation pattern is of more importance than CCHE. At a local skin temperature of 13°C only 20% is cutaneous flow, which means a reduction of 70% in heat loss when compared to the situation with a local skin temperature of more than 25°C. The contribution of CCHE to the reduction in heat loss has a maximum of 30% at a hand temperature of 25°C.
The contradictory results of several authors are due to differences in the assumptions of the analytical models. Also, verification of the models is a problem for technical reasons.

It is possible that a combination of the aforementioned responses to prevent heat loss exists. Vanggaard (1975) and Burton and Edholm (1955) supposed that the blood leaving the capillaries drains the deeper veins, while blood leaving the AVA enters the superficial venous circulation. In favour of this is the finding that the oxygen content of superficial veins is close to arterial values. The change in circulation from superficial to central in the extremities is beneficial for the efficiency of counter-current heat exchange because the distance between the arterial and venous vessels is reduced. Raman and Roberts (1989) seem not to have incorporated this phenomenon in their model, which makes their results questionable for low skin temperatures.

3 ANASTOMOSES

An anastomosis is a natural or acquired connection between two organs, spaces or parts of the same organ with each other (Holboom, 1974). In the human lymphatic and circulatory system numerous anastomoses are present. Anastomoses can be detected in the arterial network as well as in the venous network. In the venous network the superficial and deeper veins form anastomoses. In the arterial network an example of an anastomosis is the basilary artery which forms the point of connection of both vertebral arteries. In case one vertebral artery closes, the other takes over and blood can still flow to the crucial basilary artery. In this way the anastomosis forms a kind of protection. If one vessel closes and the other takes over, one vessels degenerates, while the other dilates and strengthens. Therefore, anastomoses are no fixed structures, but may come and go on demand. Clark (1938) developed a double-walled chamber in the ear of rabbits to study the development of AVA. In one chamber 41 AVA were counted 39 days after installation, of which 38 had persisted for 33 days of observation, 2 of the original 40 having subsided and 3 new ones developed.

3.1 **Arterio-venous connections**

The most common connection between the arterial and venous network is formed by the capillaries. Besides these capillaries we know the following vascular connections between the arterial and venous network (Gray, 1980):

- preferential channels,
- simple arterio-venous connections,
- specialised arterio-venous connections, also called glomera.

An almost identical classification is made by Staubesand (1950, in Hale & Burch, 1960). He distinguishes between 3 types of arterio-venous connections: bridge-anastomoses, arterio-venous connections and glomus organs. His classification is derived from Schumacher (1938, in Hale & Burch, 1960) in type I, type II anastomoses and glomera. The terminology of Gray is adopted. Clark (1938) points out that the difference between arterio-venous anastomoses and glomera was not present in that time. Masson (1937) was dissatisfied with the name 'arterio-venous anastomosis' because of the confusion with traumatic and other unusual connections which have received the same name. He adopted the term 'glomus'. This new name had the remarkable effect of a renewed interest in AVA. A few decades later a distinction was made in structure between AVA and glomera.

Preferential channels are vessels with an endothelial wall: the diameter is greater than that of capillaries: about 10 to 20 μm (Bernards & Bouman, 1978). According to Hale and Burch arterio-venous connections originate from preferential channels. They start to mark off by the development of smooth muscle cells which can regulate the blood flow by contraction. Factors related to blood flow in the skin condition the further development of these primitive anastomoses, which eventually can lead to the formation of highly developed glomus organs. The best known glomus organs are found in the bifurcation of the carotid artery and the os coccygae. In the human nail bed the AVA are so elaborated that they can also be called glomera. Glomera consist of encapsulated arterio-venous connections. In such a glomus blood vessels, muscle cells and nerve cells are present. These cells are arranged in a non-systematic way.

3.2 **Location and number of AVA**

The number of AVA in not constant. In animals the number of AVA increases as the need for local blood supply increases, and the number decreases as the stimulus is removed. According to Sinclair (1978) it is unknown if this is also true in humans. However, Hale and Burch (1960) investigated the human fingertip and made it plausible that arterio-venous anastomoses develop if blood supply induces so. Despite the variation in the number of AVA attempts are made to count the AVA. For the index finger of only 1 subject Grant and Bland (1931) found 501 AVA per square cm in the nail bed, 236 in the finger tip, 150 on the palmar side of the distal phalanx and 20 for the palmar side of the medial phalanx and 93 for the palmar side of the proximal phalanx. They found no AVA on the dorsal side of the hand. These numbers of AVA are very often cited by other authors, and very often incorrect. For instance, Hale and Burch (1960) turned the 150 AVA on the distal phalanx into 50 AVA. Although Grant and Bland claim that they found similar results in 3 other index fingers, it is

good to realise that the numbers are derived from only one index finger. Masson (1937, quoted in Clara, 1939) only counts 3 to 4 AVA per cm^2 on the top of the finger and about 10 in the nail bed. Clara (1939) argues that Grant and Bland counted the same AVA several times. AVA are very tortuous and they did not account for that in their counting technique. Therefore, it is totally wrong when Burton and Edholm (1955) state that Clara instead of Grant and Bland counted 500 AVA per cm^2 in the nail bed and 236 in the fingertips. They must have cited the wrong source. Besides, it is very strange that Hale and Burch forgot to mention the work of Clara in their very complete review of the literature concerning AVA. However, it is without doubt that the number of AVA is greater in the nail bed than on the inside of the top of the finger, and that the top of the finger has more AVA than the palm of the hand.

There are several locations in the human body where AVA are found. In the review of Hale and Burch (1960) and in Clara (1939) were mentioned: the skin of the inside of the hand and foot, elbow, lips, cheeks, ears and nose. There is some discussion about the presence of AVA in the skin of the head. Some authors (as Hoyer, 1872, quoted in Clara, 1939) were not able to detect AVA in the skin of the nose, ears and lips. Furthermore, they are found in the nail bed, corpus cavernosum of the penis of the man, ovarium of the woman, the glandula submandibularis, the kidneys, the stomach, intestines and mesenterium, and the lymph nodes. Glomera are found in the bifurcation of the carotic artery, close to the os coccygae and in the fingertips and nail bed. According to Clara (1939) probably no AVA are present in the blood supply of the central nervous system. Clark and Edholm (1985) state that there is no evidence of arterio-venous shunts being found in the blood vessels supplying the muscles. Rabbit ears do contain large numbers of AVA which are investigated thoroughly because they can be seen simply with a good light source.

Popoff (1934, quoted in Hale & Burch, 1960) was not able to find AVA in premature and newborn infants and related this finding to the poor temperature control mechanisms which are characteristic for these infants. Hale and Burch did find AVA in the newborn, supplied with smooth muscle and rejected the findings of Popoff.

The location of AVA throughout the human body are almost exclusively determined by injection with contrast fluid. The viscosity of this fluid was such that it could not pass the capillaries. If the fluid was detected in arteries after injection in the venous part, and if the fluid was detected in the veins after injection in the arterial part, it was assumed that the fluid had passed AVA. In this way only the diameter of the vessels was a criterion for the existence of an AVA. Enlarged capillaries or preferential channels are thus wrongly seen as AVA.

3.3 Anatomy and physiology

The arterio-venous anastomosis may be straight or very tortuous. In Fig. 1 an example of an arterio-venous anastomosis is given from the adult nail bed. AVA posses a thick muscular coat of peculiar structure and a relatively fine lumen, measuring 10 to 30 μm on the average (Gray, 1980). Roddie (1983) states that the average lumen is 35 μm. Under the influence of the sympathetic nervous system, which gives a rich supply of non-myelinated fibres to the wall of the vessel, they are capable of complete closure. If the AVA are open, large amounts of blood can pass. Clark (1938) calculated that the volume blood flow of opened AVA with an average diameter of 40 μm was 256 times greater than a capillary of similar length. He found that AVA (in the rabbit) rarely exceeded 50 μm inside diameter. Nelms (1963) reports a 1000 fold increase in blood flow for AVA dilated to 60 μm compared to a diameter of 10 μm. Gray points out that a closure of the AVA may not only be caused by the muscular coat, but also by a swelling of the epithelial cells.

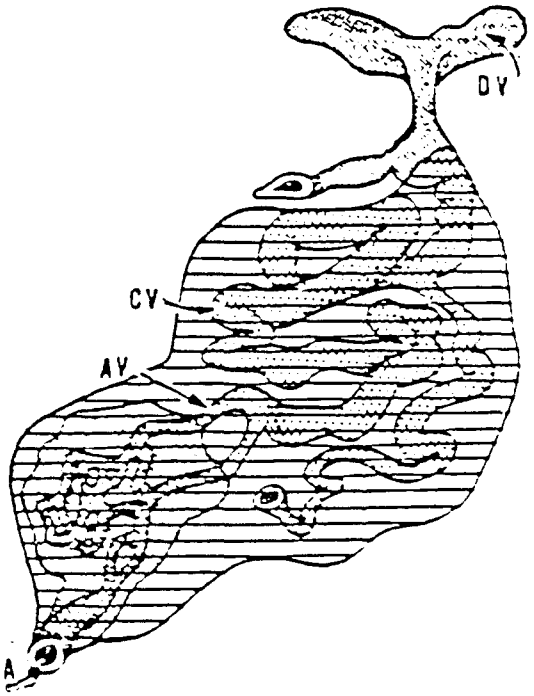

Fig. 1 Schematic drawing of a glomus organ from an adult nail bed. A is the artery, AV the arterio-venous anastomosis, CV the collecting vein, DV the dermal vein. Horizontal hatching denotes the connective tissue capsule. The anastomotic segment is encapsulated with epithelioid cells (fine stippling). From Hale and Burch (1960).

In the hands and feet AVA are organised in large numbers of small units, called glomera. Ali AVA in the hand and foot are encapsulated (Clara, 1939). The capsule consists of connective tissue covered by a rich network of vessels. In the fingers more collagen is present than in the toes.
In the extremities glomera are found in the nail bed and in the index finger. They are located deep in the dermis and nourished by one or more arteries. The afferent arteries come off at right angles from the skin arteries heading for the skin surface. A short distance from its origin the afferent artery of a glomus gives off a number of fine 'periglomeral' branches and at once becomes considerably enlarged. It makes an S-shaped curve and then narrows down to become continuous with a short funnel-shaped vein which opens at right angles, into a collecting vein. This vein begins in the middle of the glomus and curves round its outer surface. There it receives venules from the papillary layer of the skin. Finally it joins one of the deeper cutaneous veins.
It is important to note that this general description of well developed AVA does not apply to all AVA in the human body. There are large differences in structure of the AVA throughout the body, for instance in the thickness of the muscular wall and the amount of innervation.

3.4 Innervation of the circulatory system

The blood vessels in the human skin are opened and closed by hormonal and nervous influences. Several systemic hormones have an influence on vasomotor tone. However, in the acute reaction to cold the nervous system plays a predominant role. Therefore, the focus will be given to the nervous connections to the blood vessels in general and more specific the AVA.
The vast majority of the nerves to arterial and venous vessels are autonomic, but some may be sensory, for example to subserve arterial pain (Nelms, 1963). The sensory endings are mainly found close to the capillaries (Nelms, 1963).

The autonomic nervous system can be divided in a parasympathetic and sympathetic part. The parasympathetic nerves mainly transmit their impulses to the effector by acetylcholine, the sympathetic nerves by (nor)adrenaline. (Nor)adrenaline is equivalent to (nor)epinephrine.

Activation of the parasympathetic nerves results in dilatation of the vessels. The action of the sympathetic nerves depends on the receptors in the vessel wall. Stimulation of α-receptors in the vessel wall leads to vasoconstriction, while stimulation of β-receptors leads to vasodilatation. The receptors in the vessel wall can be subdivided into α_1 and α_2 or β_1 and β_2, characterized by a different reactivity to vasoactive drugs. In summary, vasodilation can be caused by stimulation of the parasympathetic system, stimulation of β-adrenoceptors (active dilatation) or by a decrease of α-stimulation (passive dilation). Vasoconstriction can be caused by stimulation of α-receptors (active vasoconstriction) or by a decrease of the activity of the β-receptors (passive vasoconstriction).

Skin

The arterioles and metarterioles in the human skin are innervated by the sympathetic as well as the parasympathetic nerves (Guyton, 1976). The nor(epinephrine) receptor is mainly of the α-type. Ekenvall et al. (1988) administered adrenoceptor antagonists into the finger skin and applied local cooling. The vasoconstriction response was abolished after administration of an α_2-adrenoceptor antagonist. They concluded that vasoconstriction is mediated in the finger by α_2-receptors.
Innervation of skin blood vessels is not identical in several places of the human body.
The blood vessels of the hand skin are normally subjected to a high degree of vasoconstrictor tone even though the subject is comfortably warm. The large increase in hand blood flow during body heating seems to be due entirely to release of vasoconstrictor tone, and there is no evidence that vasodilator fibres contribute to this increase.
In forearm skin the cutaneous vessels are not subjected to appreciable vasomotor influence when the subject is comfortably warm. Cooling the subject causes flow to fall due to vasoconstrictor fibre activity. Heating the subject causes flow to rise, and this is mediated by sympathetic fibres to the skin whose activity results in vasodilation (Roddie, 1983).
Some parts of the skin of the body are innervated like the hands (e.g. ears, lips), while other parts have similarity to the forearm-innervation (e.g. upper arm, calf and thigh).

Muscle

In the arterial part of the muscle almost no parasympathetic nerve ends are found. The predominant receptors for (nor)epinephrine are of the α- and β_2-type. This means that active vasoconstriction and active vasodilation can be accomplished. However the opening of the resistance vessels in the muscle is also very dependent on the local metabolism of the muscle cells (Shephard, 1983).

The precapillary sphincters probably have α-receptors. Receptors in the venules and veins are of both α- and β-subtype. No parasympathetic activity is shown on the venous part of the circulation.

According to Guyton (1976) the strong muscular wall of AVA is innervated by sympathetic nerves using norepinephrine as a transmitter. Nelms (1963) has a different opinion. The constrictor innervation is adrenergic sympathetic, but the anastomotic vessels dilate in response to acetylcholine and contain large amounts of specific anticholinesterase, which may indicate some sympathetic cholinergic, possibly vasodilator, innervation.
Hales and Iriki (1977) found an increased blood flow in the AVA and an almost unchanged flow through the capillaries in sheep when the central nervous system

was warmed. They concluded that alterations in blood flow through the AVA are effected by variations in sympathetic vasoconstrictor tone, and that blood flow through the capillaries might involve an axon reflex. The axon reflex originates in the somatic endings close to the capillaries (Nelms, 1963) and goes to the CNS which is in close contact with the sympathetic nervous system. The sympathetic nervous system activates the α-adrenoceptors in the precapillary sphincters and thus alters the blood flow through the capillaries.

In conclusion, the blood vessel wall of arteries, arterioles, metarterioles, AVA, venules and veins is richly innervated with nerve endings of the autonomic nervous system. It depends on the presence of parasympathetic nerves and the distribution of adrenoceptors in the wall if constriction or dilation is the primary response to local cold. The capillaries are not innervated. However, somatic endings are so close that the somatic system may play a role in the regulation of blood flow through the capillaries.

4 FUNCTION OF AVA IN THERMOREGULATION

Non-exercising humans in a cold environment try to reduce heat loss, while in a hot environment heat loss is stimulated. There are two important exceptions to this rule, both of which are related to the presence of AVA: cold induced vasodilation (CIVD) and heat induced vasoconstriction (HIVC).
The AVA are not only important in thermoregulation, but held responsible for several functions. Opening and closing of the AVA has an effect on the blood pressure and blood distribution (Ciara, 1939). Since AVA are well innervated (Clara, 1939) and because they have a topographical relation with touch sensors and free nervous endings in the skin (Clara, 1939; Hale & Burch, 1960) it is suggested that they play a functional role in touch sensation, thermoception and pain detection. There is, however, hardly any scientific evidence to support this view.

4.1 **CIVD**

Lewis described in 1930 the reduction in local skin temperature after immersion of a finger in cold water. After a few minutes the skin temperature increased again, and later the skin temperature followed cyclic periods of warming and cooling. He called this phenomenon the 'hunting' response. Later the term cold induced vasodilation (CIVD) was accepted. CIVD occurs at low environmental temperatures (Burton & Edholm, 1955). The blood flow is increased in this situation. Spealman (1945) found a blood flow of 5.9 cc per 100 cc hand volume per minute at a temperature of 35°C. At a temperature of 15°C the blood flow was only 0.9 cc per 100 cc hand volume per minute. At 5°C the blood flow had increased again to 4.3 cc per 100 cc hand volume per minute!

Ducharme and Radomski (1990) showed that CIVD did occur at relatively high temperatures in the muscles, but could hardly be demonstrated at the skin surface. CIVD starts distally in an extremity and continues in proximal direction (Aschoff, 1944).
The occurrence of CIVD decreases as the temperature of the human core decreases (Van de Linde & Romet, 1991). Therefore, it is likely that in a hypothermic subject the risk of local cold injury is increased. It is not surprising that such a high incidence of non-freezing cold injuries is reported (Francis, 1984: 38 per 1000 soldiers in WWI; Chandler, 1981: 60,000 American soldiers during WWII).
Immersion in cold water is often a painful experience. LeBlanc (1975) noted that the most painful period occurred during vasoconstriction, and that the vasodilation phase was often felt as a relief. The pain during strong vasoconstriction may be seen as a warning for strong cooling. If the cooling continues the temperature may decrease below a threshold for nerve conduction. If that threshold is reached no information from the periphery can reach the central nervous system.

In the article of Grant and Bland (1931) a relation between the number of AVA and the occurrence of CIVD is supposed. Areas which exhibit CIVD are supposed to contain many AVA. According to Lewis (1930) the CIVD areas are the feet, toes, nose, chin and probably the lower arm and elbow. Besides these locations Fox and Wyatt (1962) found CIVD in a study on various parts of the human body in the skin of the head, the neck, the olecranon and the patella, the outside of the anus, the buttocks and the skin around the nipples.
If we compare these locations with the locations of the AVA (§ 3.2) we see similarities, but certainly not a perfect correspondence. The inside of the hand and foot and parts of the face are involved in CIVD and known to have many AVA. Moreover, Aschoff shows that the fluctuations in CIVD are larger in the distal phalanx than in the proximal one. This corresponds with the distribution of AVA as reported by Grant and Bland (1931).
However, there is no mention of AVA in the skin of the buttocks, olecranon and patella. It seems interesting to investigate the presence of AVA in these regions. Aschoff (1944) states that Lewis (1930) found CIVD in the ears, in which no AVA are found.

The cause of CIVD is the subject of many theories. Lewis (1930) supposed that an axon reflex caused the opening and closing of the AVA. He found that CIVD still occurred after section and degeneration of sympathetic nerves and after section of the somatic nerves, but disappeared after degeneration of the somatic nerves. Greenfield et al. (1951) saw CIVD in several patients without somatic innervation but with reduced amplitude compared to healthy subjects. They concluded that the axon reflex was not the only explanation of the phenomenon, but that it contributed to the amplitude of the response. They did not speculate about possible other mechanisms. Aschoff (1943) in Aschoff (1944) supposed at first that cold paralysed the muscle surrounding the AVA, and that this caused

the increase in blood flow. The increase in blood flow increased the temperature, which in turn ended the paralysis. This was the explanation for the cyclic changes. Later (Aschoff, 1944) he postulated that a dilating substance (yet unknown) had to be present, which was activated when a threshold was surpassed. The increased blood flow washes the substance away. The concentration of the substance should be dependent on the temperature. Shephard et al. (1983) found that the affinity for norepinephrine of α-receptors in smooth muscle increased due to cold. This induces a strong vasoconstriction. The tissue temperature decreases and a nervous blockade occurs (norepinephrine is not released and the contractile apparatus stops). The blood flow increases again, nerve conduction is restored and the affinity for norepinephrine increases again. These consecutive changes are supposed to explain the 'hunting' phenomenon.

4.2 HIVC

The reverse of CIVD occurs too. Nagasaka et al. (1987) registered a decrease in finger blood flow with plethysmography as the water temperature increased from 37 to 43°C. This Heat Induced Vasoconstriction (HIVC) makes that a very high ambient temperature can not reach the human core easily. However, the authors find a gradual increase in finger blood flow with the laser Doppler technique under the experimental circumstances. They suppose that the latter technique is hardly capable to measure blood flow in the AVA and only limited to capillaries on the surface of the skin. This means that the blood flow through the capillaries has increased and that the blood flow through the AVA must have shown a strong decrease in the warming period.

4.3 The influence of central body temperature

Both core and local skin temperature influence the amount of contraction of the wall of the AVA. Grant (1930, quoted in Clark, 1938) found that when the temperature of a rabbit was raised the anastomoses dilated, and that they closed upon cooling. When he cooled the ear only, the AVA opened at temperatures below 15°C, the phenomenon treated under the heading CIVD.
Hales and Iriki (1977) also found in sheep that warming of the CNS produced opening of the AVA, probably due to a reduction in sympathetic stimulation. Clark and Edholm (1985) state that if body temperature of a human is raised there is a marked increase in peripheral blood flow even if local temperature remains constant. If the local temperature is decreased blood flow decreases.

5 CONCLUSION

The arterio-venous anastomoses play an important role in thermoregulation. If the strong muscular wall relaxes an enormous amount of blood can pass through. The heat warms the skin and reduces the risk of cold injury in that part of the skin.
The muscular wall of AVA is richly innervated with sympathetic nerves. The muscle wall is predominantly equipped with α-adrenoceptors. This means that activation of the sympathetic system leads to active vasoconstriction and a decrease in sympathetic activity to passive vasodilation. Cold increases the affinity of the receptors for noradrenaline. This means that the AVA close in cold environments. This in turn affects the tissue temperature, which can become so low that the contractile apparatus of the smooth muscle stops working due to nervous blockade of the sympathetic nerves. Thus the phenomenon of CIVD can be explained.
If the tissue temperature is close to the core temperature the sensitivity of the adrenoceptors is reduced and the AVA are opened. If the tissue temperature exceeds the core temperature as in the experiments of Nagasaka et al. (1987) the AVA close again. The mechanism behind this phenomenon (HIVC) is still unexplained but a possible explanation may be an increase in sympathetic activity. This increase may be a result from an axon reflex originating in the somatic endings close to the capillaries.

6 RECOMMENDATIONS

Research on the phenomenon of CIVD is far more elaborated than on the phenomenon of HIVC. The exact mechanism of HIVC deserves further attention, and may improve the knowledge on the function of the AVA.
One very important aspect is hardly noted in the literature: the relation between body temperature and opening of the AVA. Till now all emphasis is laid on local mechanisms.
Many authors make almost no distinction between capillary blood flow and blood flow through the AVA. It is important to quantify which kind of flow is determined with a certain technique.
There is no perfect correspondence between the sites where CIVD occurs and the sites were AVA are demonstrated. A thorough search for AVA on the sites where Fox and Wyatt (1962) found CIVD, may clarify if AVA are the sole explanation for the occurrence of CIVD.
The sites of AVA are often determined with an injection technique which is subject to errors. A reexamination of these sites with a more reliable histological technique is recommended.

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15. ABSTRACT (MAXIMUM 200 WORDS, 1044 BYTE)

In a cold environment human heat loss is reduced by peripheral vasoconstriction, counter-current heat exchange and a change of the peripheral circulation pattern. However, these mechanisms go at the expense of the tissue temperature in the extremities. The cooling can be so pronounced that local cold injuries occur. Cold induced vasodilation (CIVD) may be regarded as an effective protection against local cold injury. The underlying mechanism is often associated with the presence of arterio-venous anastomoses (AVA). Rhythmic relaxation and contraction of the strong muscular wall of the AVA is often supposed to cause the 'hunting' response in CIVD. The contraction phase is probably caused by stimulation of the α-adrenoceptors in the smooth muscle wall. Relaxation may be caused by a nervous blockade of the sympathetic system. There is no scientific evidence for humeral mediators. The influence of the body temperature on the vasomotor tone of the AVA remains to be investigated. The locations of AVA and the sites where CIVD occurs are not in perfect correspondence and also this point needs further research.

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